



Developing a Proposed Regulation for Genetic Testing under CLIA

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Clinical Laboratory Improvement Amendments (CLIA) Regulations

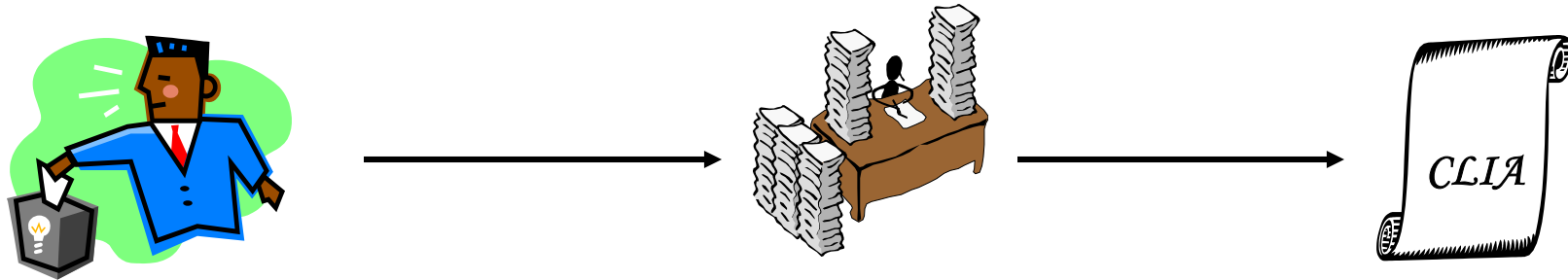
- Apply to all laboratories performing clinical testing
- Based on complexity structure
- For non-waived testing - include requirements for PT, facilities, quality systems, and laboratory personnel
- Minimum standards



CLIA Oversight

- **Centers for Medicare & Medicaid Services (CMS)**
 - **Publish regulations**
 - **Administer CLIA program**
- **Centers for Disease Control and Prevention (CDC)**
 - **Conduct assessment studies**
 - **Convene CLIAC meetings**
 - **Provide scientific and technical support/consultation**
- **Food and Drug Administration (FDA)**
 - **Complexity categorization**
 - **Waiver determinations**

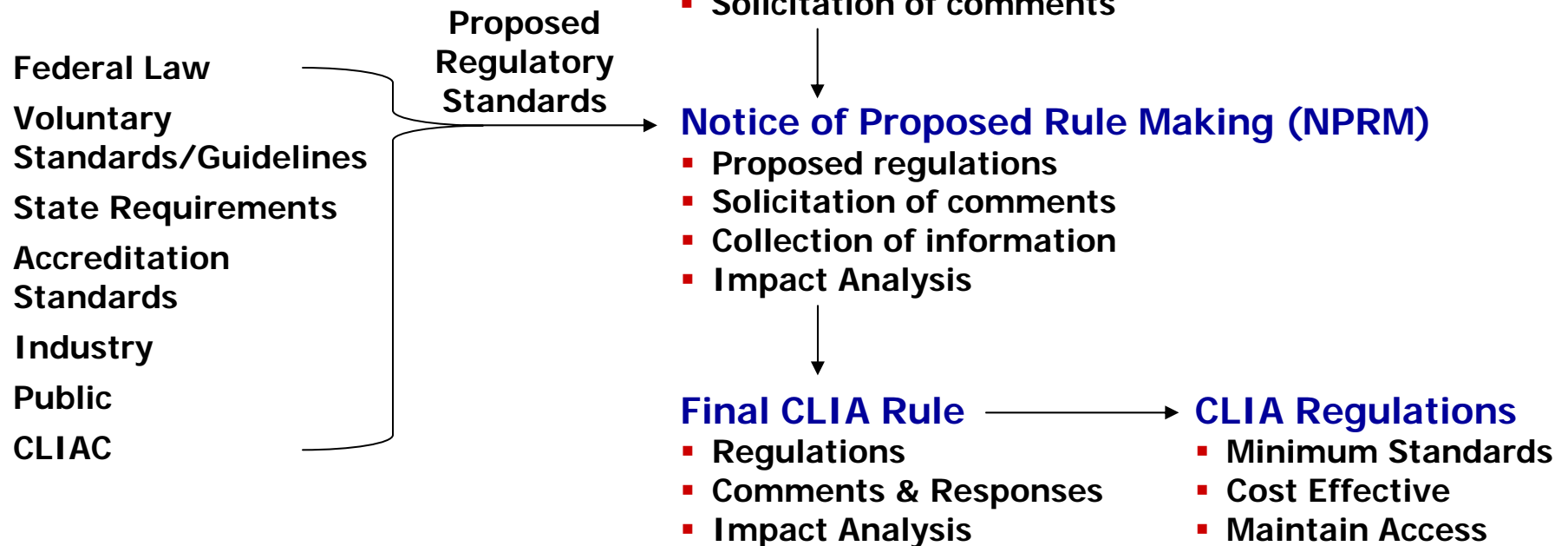
CLIA Standards Development



INPUT

PROCESS
(RULEMAKING)

OUTPUT





Current CLIA Requirements Applicable to Genetic Testing

- General requirements for non-waived testing
- Specialty of clinical cytogenetics
 - Specific QC requirements
 - Qualification requirements for technical supervisor
- Requirements for molecular amplification procedures
- No specific requirements for genetics, molecular genetics or biochemical genetics



CLIAAC Recommendations

- **1997 – NIH/DOE task force report**
- **1997 – CLIAAC considered how CLIA applies to genetic testing**
- **1998 – CLIAAC recommended changes to CLIA**
- **1999 – SACGT supported CLIAAC recommendations**
- **5/2000 – Notice of Intent (NOI) seeking public comment on CLIAAC recommendations**



NOI Issues for Comments

- Definition and categories
- Clinical validity
- Authorized person
- Informed consent
- Confidentiality
- Genetic counseling
- Pre-analytic, analytic, and post-analytic issues
 - **Test requisition, retention and use of tested specimens**
 - **Quality control, test validation, and proficiency testing**
 - **Test report and record retention**
 - **Personnel qualifications and responsibilities**



Public Comments on NOI

- 57 comment letters containing over 800 comments
- Issues receiving most comments:
 - **Definition and subspecialties of genetic testing**
 - **Documentation of clinical validity**
 - **Individuals authorized to order genetic tests**
 - **Informed consent**
 - **Laboratory's role in providing consultation and genetic counseling**
 - **Requirements related to the pre-analytic phase**
 - **Personnel qualifications and responsibilities**



Examples of NOI Comments

Definitions of Genetic Testing

- Most commenters supported creation of a specialty
- ~ 50% felt definitions too broad
- Major issues:
 - Germ-line mutation vs. acquired or somatic mutation testing
 - Determination of a test as “genetic”
 - Intended use
 - Subspecialties
 - Newborn screening
 - Maternal serum screening
 - HLA testing
 - Pharmacogenetic testing
 - Parentage testing



Examples of NOI Comments (cont.)

Clinical Validity

- ~50% commenters disagreed with NOI proposal
- ~50% requested clarification of clinical validity
- Differing positions
 - Impractical and out of laboratory's purview
 - Should be laboratory's responsibility to review existing data
 - Should not be required for all laboratory tests
 - Should be required only for certain types of tests
 - Should be an ongoing process following introduction into clinical practice
- Concerns about monitoring, criteria, availability, data sources, number of samples to be tested



Examples of NOI Comments (cont.)

Informed Consent

- ~60% felt laboratories should not be required to ensure documentation of informed consent
- Most believed health care providers should be responsible
- Some suggested CLIA as appropriate mechanism to regulate informed consent
- Most felt oversight should be deferred to states
- Laboratories should be required to establish policies and procedures
- Controversy on extent of laboratory responsibility



Revised CLIAC Recommendations

- **9/2000 – CLIAC reviewed NOI comments analysis and formed Second CLIAC Genetics Workgroup**
- **12/2000 – Genetics Workgroup meeting**
- **2/2001 – CLIAC revised recommendations and recommended development of a proposed rule**



Development of CLIA Proposed Rule for Genetics

- Major issues under consideration
 - Definitions of genetic testing and subspecialties
 - Informed consent
 - Test validation
 - Proficiency testing
 - Subspecialty requirements
 - Retention and use of tested specimens
 - Personnel qualifications



Principles in Developing Proposed Rule

- **Ensure quality of all phases of genetic testing**
- **Provide flexibility to accommodate different testing environments and processes**
- **Ensure appropriate qualifications for laboratory personnel**
- **Assure availability of, or access to, quality genetic testing**



Developing Proposed Rule

- **Input for proposed requirements**
 - CLIAC recommendations
 - Public comments
 - Voluntary standards and guidelines
 - Accreditation standards and checklists
 - State requirements
 - Other Federal requirements
 - Input from government agencies
- **Modification of proposed requirements occurs through rule making process**



NPRM Content

- **Preamble**
 - Explanation/clarification of proposed requirements
 - Comments and responses
 - Collection of information
 - Regulatory impact analysis
- **Proposed requirements**



Regulatory Impact analysis (RIA)

- Assessment of potential impact of proposed requirements
 - Potentially affected entities
 - Laboratories performing genetic testing
 - Accreditation and State programs
 - Industry
 - Others
 - Test volumes
 - Volume of genetic tests in each proposed subspecialty
 - New test implementation rates
 - Current laboratory practice in genetic testing
 - Genetic testing personnel
- Cost-benefit analysis
 - Quantify potential costs and benefits
 - Project costs and benefits over five years



Information for RIA

- **Identification of available information sources**
 - **CDC studies**
 - **CMS data**
 - **Exempt States (NY, WA)**
 - **Government reports**
 - **Literature references**
 - **Industry reports**
 - **Data and information from professional groups**
 - **GeneTests**
 - **New England Newborn Screening Program**
 - **Experts in laboratory testing and health economics**



Status of NPRM

- ✓ Revised CLIAC recommendations
- ✓ Voluntary Standards/Guidelines
- ✓ State Requirements
- ✓ Accreditation Standards
- ✓ Industry
- ✓ Public

NOI

- CLIAC recommendations
- Solicitation of Comments

- ❖ Proposed Regulatory Requirements
- ❖ Information Collection
- ❖ Regulatory Impact Analysis
- ❖ Clearance

NPRM

- Proposed regulations
- Solicitation of Comments
- Collection of information
- Impact Analysis



Final Rule

- Regulatory Requirements
- Comments & Responses
- Collection of information
- Impact Analysis



Questions???

